=> file casreact
FILE 'CASREACT' ENTERED AT 16:04:42 ON 10 JUN 2008

FILE CONTENT:1840 - 7 Jun 2008 VOL 148 ISS 24

New CAS Information Use Policies, enter HELP USAGETERMS for details.

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* CASREACT now has more than 13.8 million reactions *
*
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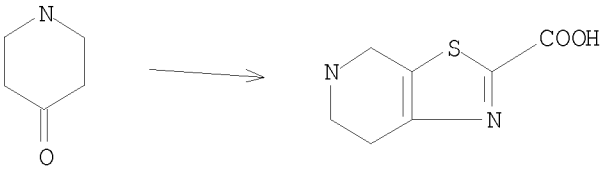
Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que
L1 STR

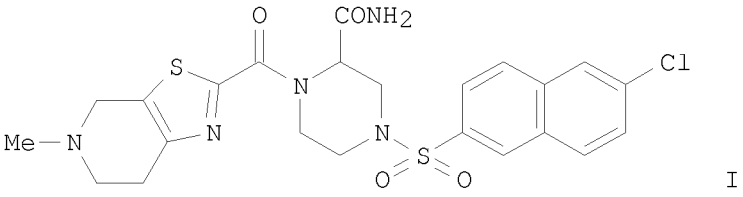


Structure attributes must be viewed using STN Express query preparation.
L3 3 SEA FILE=CASREACT SSS FUL L1 (5 REACTIONS)

=> d l3 1-3 ibib abs hit

L3 ANSWER 1 OF 3 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 141:395464 CASREACT
TITLE: Synthesis and Conformational Analysis of a Non-Amidine Factor Xa Inhibitor That Incorporates 5-Methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine as S4 Binding Element
AUTHOR(S): Haginoya, Noriyasu; Kobayashi, Syozo; Komoriya, Satoshi; Yoshino, Toshiharu; Suzuki, Makoto; Shimada, Takashi; Watanabe, Kengo; Hirokawa, Yumiko; Furugori, Taketoshi; Nagahara, Takayasu
CORPORATE SOURCE: Medicinal Chemistry Research Laboratory, Daiichi Pharmaceutical Co. Ltd, Edogawa-ku, Tokyo, 134-8630, Japan
SOURCE: Journal of Medicinal Chemistry (2004), 47(21), 5167-5182

CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

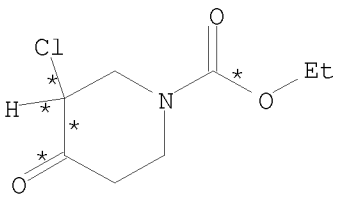


I

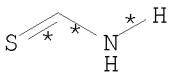
AB Our exploratory study was based on the concept that a non-amidine factor Xa (fXa) inhibitor is suitable for an orally available anticoagulant. We synthesized and evaluated a series of N-(6-chloronaphthalen-2-yl)sulfonylpiperazine derivs. incorporating various fused-bicyclic rings containing an aliphatic amine expected to be S4 binding element. Among this series, 5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine type I displayed orally potent anti-fXa activity and evident prolongation of prothrombin time (PT) with the moderate bioavailability in rats. The X-ray crystal anal. afforded an obvious binding mode that 5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine and 6-chloronaphthalene resp. bound to S4 and S1 subsites. In this X-ray study, we discovered a novel intramol. S-O close contact. Ab initio energy calcns. of model compds. deduced that conformers with the most close S-O proximity were most stable. The Mulliken population anal. proposed that this energy profile was caused by both of electrostatic S-O affinity and N-O repulsion. The results of these calcns. and X-ray anal. suggested a possibility that the restricted conformation effected the affinity to S4 subsite of fXa.

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(150) OF 352 COMPOSED OF RX(23), RX(24), RX(25)
RX(150) BY + BZ + B + BR ===> CD



BY



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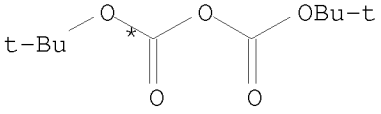

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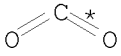
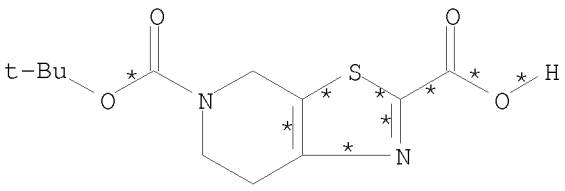


BR

3 STEPS



CD
YIELD 82%

RX(23) RCT BY 89424-04-4, BZ 115-08-2
PRO CA 165948-22-1
SOL 71-36-3 BuOH
CON 2.5 hours, 100 deg C
NTE molecular sieves used

RX(24) RCT CA 165948-22-1

STAGE(1)
RGT N 1310-73-2 NaOH
SOL 7732-18-5 Water
CON SUBSTAGE(1) 2 hours, 110 deg C
SUBSTAGE(2) 110 deg C -> room temperature

STAGE(2)
RCT B 24424-99-5
SOL 67-56-1 MeOH
CON 2 hours, room temperature

STAGE(3)
RGT AH 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature, pH 2 - 3

PRO CC 165948-24-3

RX(25) RCT CC 165948-24-3

STAGE(1)
RGT BT 109-72-8 BuLi
SOL 60-29-7 Et2O, 110-54-3 Hexane
CON 15 minutes, -78 deg C

STAGE(2)
RCT BR 124-38-9
CON 5 minutes, -78 deg C

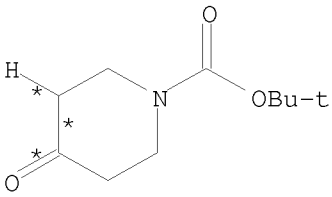
PRO CD 365996-70-9

L3 ANSWER 2 OF 3 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 141:225377 CASREACT

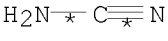
TITLE: Facile methods for preparation of thiazolopyridine and tetrahydrothiazolopyridine derivatives
AUTHOR(S): Haginoya, Noriyasu; Komoriya, Satoshi; Osanai, Ken; Yoshino, Toshiharu; Nagata, Tsutomu; Nagamochi, Masatoshi; Muto, Ryo; Yamaguchi, Mitsuhiro; Nagahara, Takayasu; Kanno, Hideyuki
CORPORATE SOURCE: Medicinal Chemistry Research Laboratory, Daiichi Pharmaceutical Co., Ltd, Tokyo, 134-8630, Japan
SOURCE: Heterocycles (2004), 63(7), 1555-1561
CODEN: HTCYAM; ISSN: 0385-5414
PUBLISHER: Japan Institute of Heterocyclic Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Improved routes to prepare tetrahydrothiazolo[5,4-c]pyridine-2-carboxylic acid lithium salts were developed. Route A consisted of the improved preparation of thiazolopyridine intermediates, and Route B is applicable for a large scale synthesis of tetrahydrothiazolo[5,4-c]pyridine-2-carboxylic acid derivs. The methods may serve as facile means for preparing thiazolopyridine and tetrahydrothiazolopyridine derivs.

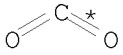
RX(31) OF 33 COMPOSED OF RX(9), RX(10), RX(13)
RX(31) V + W + S ===> AO



V

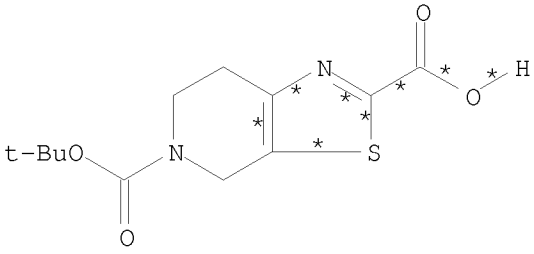


W



S

3 STEPS



● Li

AO
YIELD 66%

RX(9) RCT V 79099-07-3

STAGE(1)
RGT Y 123-75-1 Pyrrolidine

CAT 104-15-4 TsOH
SOL 110-82-7 Cyclohexane
CON 2 hours, reflux

STAGE(2)
RCT W 420-04-2
RGT D 10544-50-0 S8
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 5 hours, 0 deg C

PRO X 365996-05-0
NTE scalable, >100 g

RX(10) RCT X 365996-05-0
RGT AD 540-80-7 t-BuONO, AE 7789-45-9 CuBr2
PRO AC 365996-06-1
SOL 68-12-2 DMF
CON SUBSTAGE(1) 50 deg C
SUBSTAGE(2) 2 hours, 50 - 60 deg C
NTE scalable, >100 g

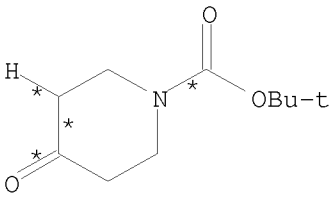
RX(13) RCT AC 365996-06-1

STAGE(1)
RGT C 109-72-8 BuLi
SOL 60-29-7 Et2O, 110-54-3 Hexane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C

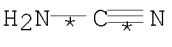
STAGE(2)
RCT S 124-38-9
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature

PRO AO 365996-70-9

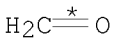
RX(33) OF 33 COMPOSED OF RX(9), RX(10), RX(11), RX(12)
RX(33) V + W + AF + S ===> U



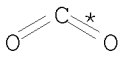
V



W

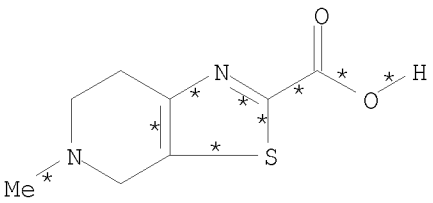


AF



S

4 STEPS



● Li

U
YIELD 99%

RX(9) RCT V 79099-07-3

STAGE(1)
RGT Y 123-75-1 Pyrrolidine
CAT 104-15-4 TsOH
SOL 110-82-7 Cyclohexane
CON 2 hours, reflux

STAGE(2)
RCT W 420-04-2
RGT D 10544-50-0 S8
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 5 hours, 0 deg C

PRO X 365996-05-0
NTE scalable, >100 g

RX(10) RCT X 365996-05-0
RGT AD 540-80-7 t-BuONO, AE 7789-45-9 CuBr2
PRO AC 365996-06-1
SOL 68-12-2 DMF
CON SUBSTAGE(1) 50 deg C
SUBSTAGE(2) 2 hours, 50 - 60 deg C
NTE scalable, >100 g

RX(11) RCT AC 365996-06-1

STAGE(1)
RGT AH 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2
CON 10 minutes, room temperature

STAGE(2)
RCT AF 50-00-0
RGT AI 56553-60-7 Na.(AcO)3BH, AJ 121-44-8 Et3N, AK 64-19-7 AcOH
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1 hour, room temperature

STAGE(3)

RGT AL 1310-73-2 NaOH
SOL 7732-18-5 Water
CON room temperature

PRO AG 143150-92-9
NTE scalable, 50 g

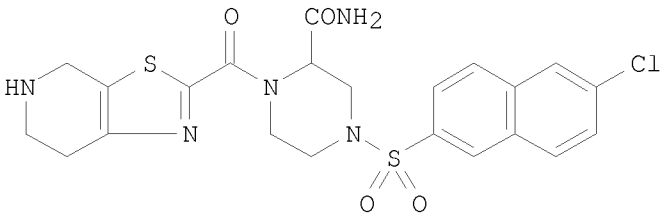
RX(12) RCT AG 143150-92-9

STAGE(1)
RGT C 109-72-8 BuLi
SOL 60-29-7 Et2O, 110-54-3 Hexane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C
SUBSTAGE(3) 20 minutes, 0 deg C
SUBSTAGE(4) 0 deg C -> -78 deg C

STAGE(2)
RCT S 124-38-9
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature

PRO U 259809-25-1
NTE scalable, 50 g

L3 ANSWER 3 OF 3 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 141:123587 CASREACT
TITLE: Orally active factor Xa inhibitors: 4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine derivatives
AUTHOR(S): Haginoya, Noriyasu; Kobayashi, Syozo; Komoriya, Satoshi; Hirokawa, Yumiko; Furugori, Taketoshi; Nagahara, Takayasu
CORPORATE SOURCE: Medicinal Chemistry Research Laboratory, Daiichi Pharmaceutical Co. Ltd., Edogawa-ku, Tokyo, 134-8630, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(11), 2935-2939
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



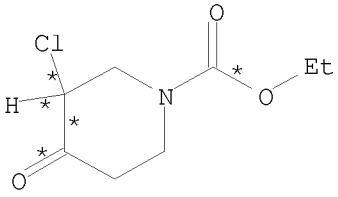
I

AB In an investigation of factor Xa inhibitors, a series of 1-(6-chloronaphthalen-2-yl)sulfonyl-4-(4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carbonyl)piperazines were synthesized. In vitro inhibitory activities of the compds. against factor Xa and coagulation are

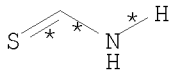
summarized. Among these, 4-[(6-chloro-2-naphthalenyl)sulfonyl]-1-[(4,5,6,7-tetrahydro-5-methylthiazolo[5,4-c]pyridin-2-yl)carbonyl]-2-piperazinecarboxamide (I) and 4-[(6-chloro-2-naphthalenyl)sulfonyl]-N-methyl-1-[(4,5,6,7-tetrahydro-5-methyloxazolo[5,4-c]pyridin-2-yl)carbonyl]-2-piperazinecarboxamide, possessing a carbamoyl or N-methylcarbamoyl moiety, showed potent inhibitory activities when administered orally to rats.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(61) OF 188 COMPOSED OF RX(3), RX(4), RX(1)
RX(61) L + M + P + B ===> C



L



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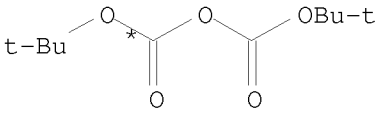

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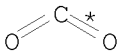
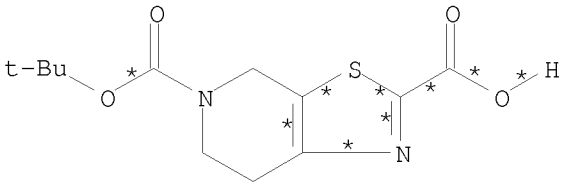


B

3
STEPS



● Li

C
YIELD 85%

RX(3) RCT L 89424-04-4, M 115-08-2
PRO N 165948-22-1
SOL 64-17-5 EtOH
NTE 4Å MS used

RX(4) RCT N 165948-22-1

STAGE(1)
RGT Q 121-44-8 Et3N
SOL 7732-18-5 Water

STAGE(2)
RCT P 24424-99-5

PRO A 165948-24-3

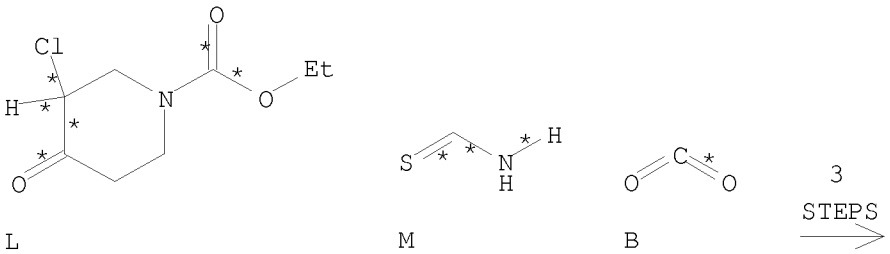
RX(1) RCT A 165948-24-3

STAGE(1)
RGT D 109-72-8 BuLi
SOL 60-29-7 Et2O

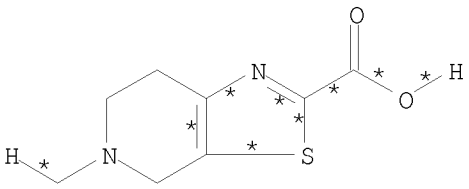
STAGE(2)
RCT B 124-38-9

PRO C 365996-70-9

RX(62) OF 188 COMPOSED OF RX(3), RX(5), RX(25)
RX(62) L + M + B ===> F



L M B



● Li

F
YIELD 100%

RX(3) RCT L 89424-04-4, M 115-08-2
PRO N 165948-22-1
SOL 64-17-5 EtOH
NTE 4Å MS used

RX(5) RCT N 165948-22-1
RGT T 16853-85-3 LiAlH4
PRO S 259809-24-0
SOL 60-29-7 Et2O

```
RX(25)    RCT  S 259809-24-0

            STAGE(1)
               RGT  D 109-72-8 BuLi
               SOL  60-29-7 Et2O

            STAGE(2)
               RCT  B 124-38-9

          PRO  F 259809-25-1

=>
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